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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/012,194	12/06/2001	Manuela Martins-Green	407E-914500US	5287

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	10/012,194	MARTINS-GREEN ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,9-16,18-20,23,25,26 and 43-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6,9-15,18-20,23,25,26 and 43-45* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 June 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 2-6, 9-16, 18-20, 23, 25, 26, 43-45 are pending in the application.

This Office Action is in response to the Amendment filed on 12/6/04.

Response to Amendment

The rejection of claims 2-6, 9-20, 23, 25, 26, 43-45 under 35 U.S.C.112 1st paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 2-6, 9-15, 18-20, 23, 25, 26, 43-45 under 35 U.S.C.103 (a) is maintained for reasons set forth of the record mailed on and further discussed below.

Claims 9, 13 and 14 are rejected under 35 U.S.C.112 2nd paragraph for reasons discussed below.

Drawings

In response to the objection of the drawing, Applicants point out the Figure 11 was present in Appendix A to the originally specification. The examiner accepts the drawing of Figure 11. However, the objection should be directed to Figure 12, which is on page 11 of the drawing filed on 6/4/04. Figure 12 is not acceptable because it is not present in the original specification, including Appendix A, therefore, it constitutes new matter.

Response to Arguments

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 13 and 14 under 35 U.S.C.103 (a) in view of Black and Li has been withdrawn in view of the new grounds of rejection necessitated by Applicant's amendment of the claims (see new grounds of rejection below).

Claims 2-6, 11, 12, 15, 18-20, 23, 25, 26, 43 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black, in view of Montesano et al.

In response to this rejection, Applicants argue that claim 23 requires mixing of connective tissue cells with a support matrix and layering the mixture on either side of an endothelial cell layer, which is not taught in either of the references. Applicants argue that Black only teaches the use of fibroblasts on top of a support matrix whereas Montesano et al. do not teach connective tissue. Applicants assert that the combined teaching of both references fails to teach every element of the claimed invention. Applicants thus conclude that the claims are patentable over the cited references by virtue of their dependence of claim 23.

The above argument has been fully considered but deemed unpersuasive. Claim 23 is a product by process claim which is drawn to a product, an artificial tissue comprising two layers of support matrix-connective tissue mixture separated by a layer of endothelial cells, wherein said endothelial cells contact inner surfaces of the support matrix-connective tissue mixture layers. The process of how this artificial tissue is made does not give further limitation to the claim. The specification does not set any definition for the term "support matrix-connective tissue mixture." As such, this term is not limited to the example set forth in the Example of the specification. It can be interpreted as "a mix of" or "placing together" a support matrix and connective tissue regardless whether the support matrix is on top, bottom or mixed prior to the formation of a support (mixture means a portion of matter consisting of two or more components

in varying proportions that retain their own properties, see Merriam-Webster dictionary). Black reference teaches adding the fibroblast, connective tissue cells, to the support matrix made of collagen, thereby form a support matrix-connective tissue mixture, which is well within the meaning encompassed by such term. Absent evidence from the contrary, the combined teaching of Black and Montesano teaches every limitation of claim 23, thus they render the claimed invention obvious. Since Applicants have not pointed out any other alleged deficiencies in this rejection, this rejection is maintained for same reasons as set forth in the previous office action (mailed on 9/2/04) and discussed above.

Claim 9 is rejected under 35 U.S.C.103 (a) as being unpatentable over Black, in view of Montesano and Li.

In response to this rejection, Applicants present the same argument as above. Applicants argue that none of the cited references teaches the limitation of mixing of connective tissue cells with a support matrix and layering the mixture on either side of an endothelial cell layer. Applicants thus conclude that the claimed invention is patentable over the cited references.

This argument has been fully considered and deemed unpersuasive. The combined teaching of Black and Montesano teaches every limitation of claim 23 for reasons discussed above. Since Applicants have not pointed out any other alleged deficiencies in this rejection, this rejection is maintained for same reasons as set forth in the previous office action (mailed on 9/2/04) and discussed above.

Claims 2, 10, 23 and 44 are rejected under 35 U.S.C.103 (a) as being unpatentable over Black, in view of Montesano et al. and Lokeshwar et al.

In response to this rejection, Applicants present the same argument as above. Applicants argue that the combination of Black and Montesano fails to teach or suggest "mixing together a support matrix and connective tissue cells to form a support matrix-connective tissue mixture and forming a culture comprising two layers of support matrix-connective tissue mixture separated by a layer of endothelial cells" as recited in claim 23. Applicants argue that Lokeshwar does not teach of suggest artificial tissue including a support matrix, together with multiple cell types recited in the pending claims, thus fails to remedy the deficiency of the Black/Montesano combination. Applicants thus conclude that the claimed invention is patentable over the cited references.

This argument has been fully considered and deemed unpersuasive. The combined teaching of Black and Montesano teaches every limitation of claim 23 for reasons discussed above. Since Applicants have not pointed out any other alleged deficiencies in this rejection, this rejection is maintained for same reasons as set forth in the previous office action (mailed on 9/2/04) and discussed above.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black et al., in view of Montesano and Li et al.

Black et al. teach a skin equivalent preparation comprising human keratinocytes plated on endothelial dermal equivalent or endothelial fibroblast dermal equivalent mixed with collagen (see page 1333, 1st col., 2nd and 3rd paragraph). Black et al. also teach that the endothelial fibroblast dermal equivalent comprising fibroblast and HUVEC (see page 1333, 1st col., 2nd paragraph). Black et al. further teach that a network of capillary-like tubular structures is formed in the tissue (see page 1333, 2nd col., 3rd and 5th paragraph). Furthermore, Black et al. teach that said tissue produces laminin, type IV collagen and extracellular matrix (see page 1334, 1st col., 2nd paragraph, and Figures 1, 2 and 3). Moreover, Black et al. disclose that said tissue is self maintained *in vitro*, and is suitable for tissue graft (see page 1338, entire 1st col., and 2nd col., 2nd paragraph).

However, Black et al. do not teach an artificial tissue comprising two layers of support matrix-connective tissue mixture separated by a layer of endothelial cells. Black et al. do not teach the artificial tissue comprising Vitrogen.

Montesano et al. teach endothelial cell monolayers established on the surface of collagen matrix and covered with another layer of collagen matrix induces the endothelial cells to reorganize into a network of branching and anastomosing capillary-like tubes resembling capillary beds *in vivo* (see page 1649, 2nd col., 3rd paragraph, lines 1-4). Montesano et al. further teach that an appropriate topological relationship of endothelial cells with collagen matrices, similar to that occurring in vivo, has an inductive role for endothelial cells to form vessel-like structures *in vitro* (see abstract).

Li et al. teach that Vitrogen, a trademark name for type I collagen, is purchased from Collagen Corp.

It would have been obvious to one of ordinary skill in the art to make an artificial skin equivalent as taught by Black et al. and introduce a second layer of connective tissue on top of the endothelial cell based on the teaching of Montesano et al. One of ordinary skill in the art would have been motivated to do so because it would resemble the capillary bed *in vivo* and thus induce capillary formation closely resemble that of *in vivo* setting, as demonstrated by Montesano et al. It would also have been obvious to one of ordinary skill in the art to use Vitrogen to make the artificial tissue as claimed based on the teaching of Black et al., Montesano et al. and Li et al. Both Black and Montesano teach using collagen as support matrix. Since Vitrogen is a trademark for collagen commonly used in cell culture, one of ordinary skill in the art would just purchase it and use it in the experiment making the artificial tissue. The level of skill in the art is high. Absent evidence from the contrary, one of ordinary skill in the art would have reasonable expectation of success to make an artificial skin equivalent as taught by Black et al., and introduce a second layer of connective tissue on top of the endothelial cells, wherein Vitrogen is used as support matrix. Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9, 13 and 14 contain the trademark/trade name Vitrogen. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe collagen and, accordingly, the identification/description is indefinite.

Claim Objections

Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
PATENT EXAMINER